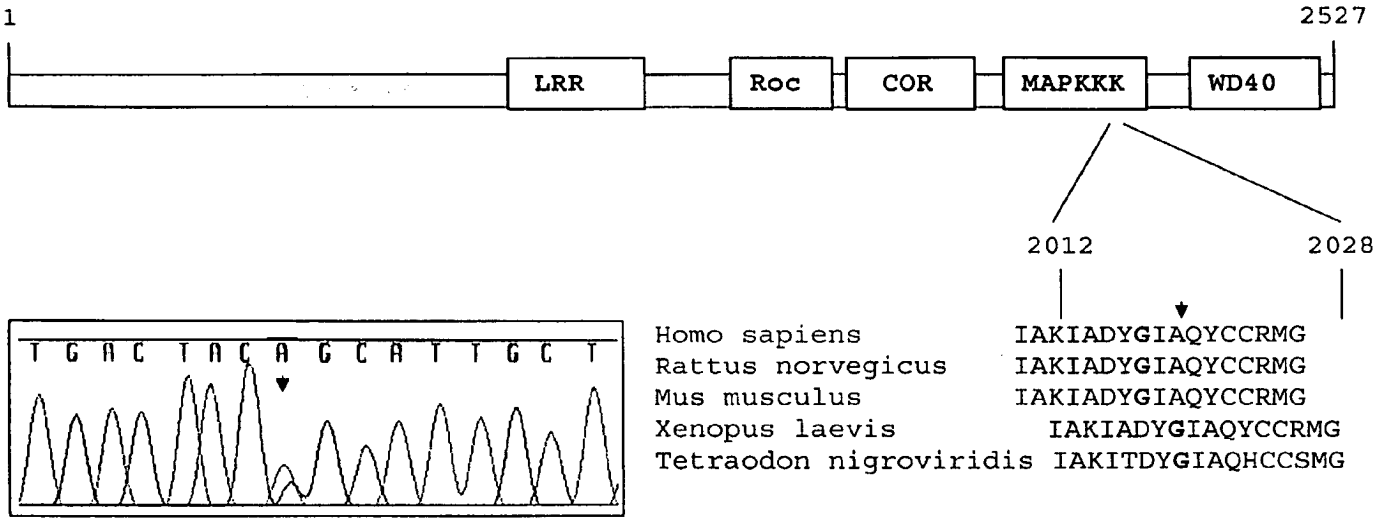


Figure 1. Schematic drawing of *LRRK2* with predicted protein domains

(LRR – leucine rich repeat, Roc – Ras in complex proteins, COR – domain C-terminal of Roc, MAPKKK – mitogen-activated protein kinase kinase kinase, WD40 – WD40 repeats). The human *LRRK2* protein sequence in the region of the G2019S mutation is aligned with orthologs from rat (XP_235581), mouse (AAH34074), frog (AAH76853), and puffer fish (CAG05593). The chromatogram shows the 6055G>A transition (G2019S)

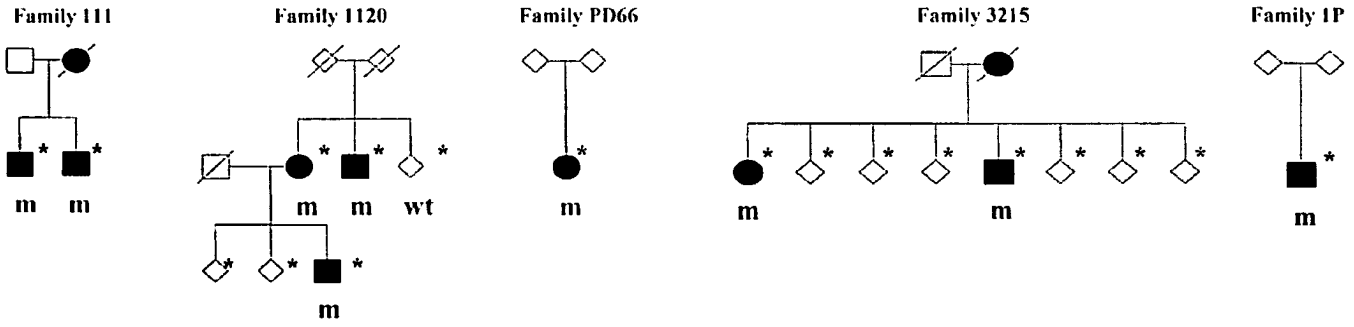
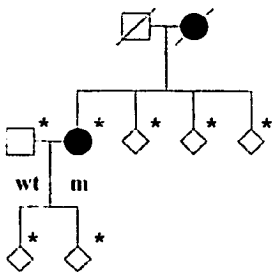


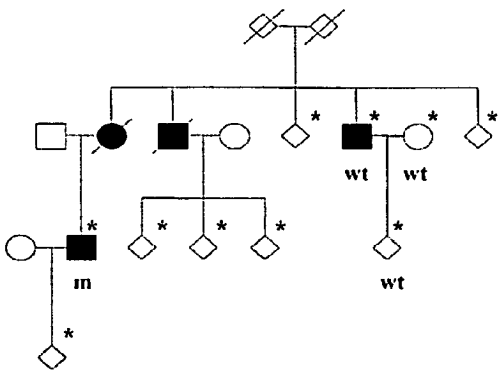
Figure 2. Pedigrees of families with *LRRK2* G2019S

□ and○ denotes sexes, and ◊ denotes that the sex is not given. A diagonal line across the symbol denotes that the person is dead, and thus that he/she has not been tested. Blackened symbols denote affected family members with parkinsonism. An asterisk denotes genotyped individual, with "m" for mutation carriers and "wt" for wild-type *LRRK2*. To protect confidentiality, the genotypes and genders of some unaffected individuals are not shown.

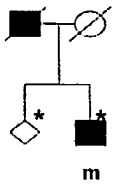
Family P-063



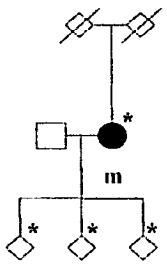
Family P-089



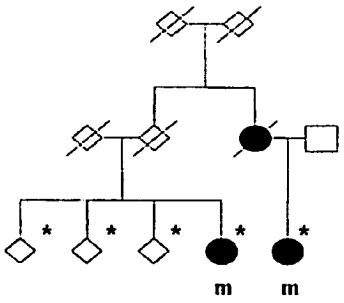
Family P-104



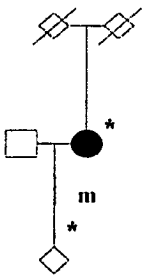
Family P-241



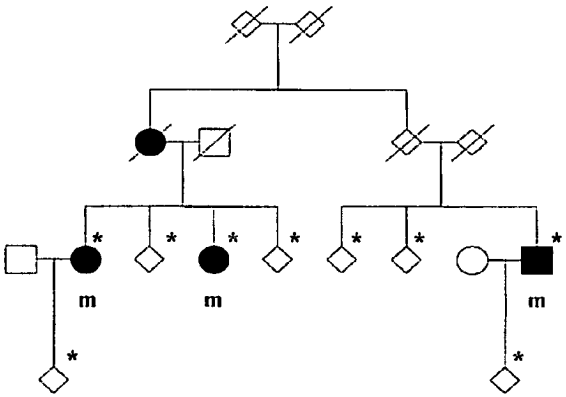
Family P-369



Family P-394



Family F05



Family 1210

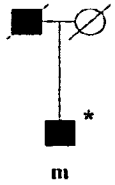
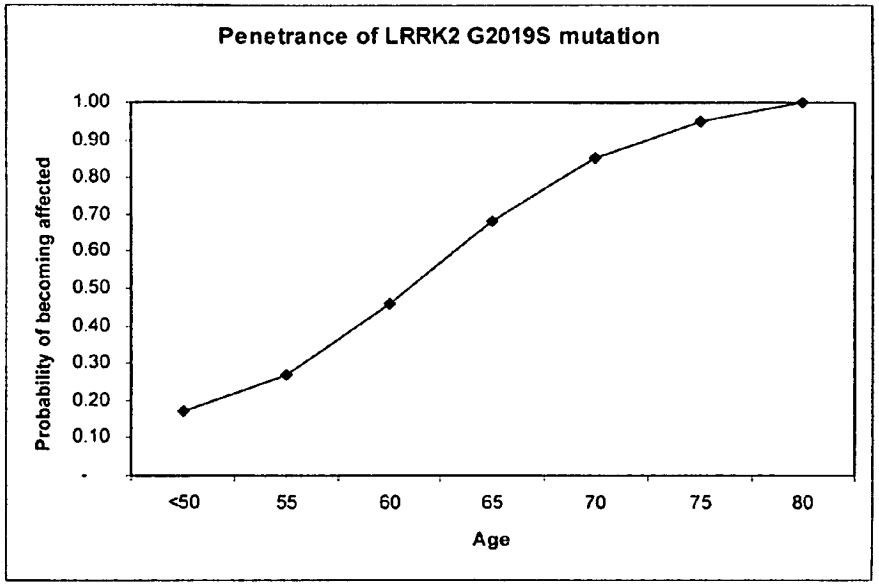


Figure 3. Chromosome 12q12 STR markers on the disease haplotype (PARK8).

	Family proband												
Marker	**P-063**	**P-089**	**P-104**	**P-241**	**P-369**	**P-394**	**F05**	**1210**	**1120**	**111**	**3215**	**PD66**	**1P**
D12S87	160	160	164	164	-	156	166	156/158	164	160	158	156/166	156/158
D12S1648	120	120	122	122	122	110	110	122/124	110	110	110	120/134	128/130
D12S2080	188	188	188	188	188	188	188	184/192	188	180	184	188/192	184/188
D12S2194	265	265	265	265	265	265	261	253/261	257	257	253	245/249	249/261
-31Kb	290	290	290	290	290	290	290	290/290	290	290	290	290/293	284/290
LRRK2_69Kb	223	223	223	223	223	223	223	219/223	223	223	223	215/215	211/219
LRRK2_84Kb	253	253	253	253	253	253	253	253/253	253	253	253	253/253	253/253
LRRK2_129Kb	151	151	151	151	151	151	151	151/151	151	151	151	151/151	151/151
212Kb	132	132	132	132	132	132	132	132/132	132	132	132/138	132/138	132/134
243Kb	315	315	315	315	315	315	315	315/315	315	315	315/309	315/312	315/300
378Kb	189	189	189	189	189	189	189	189/193	193	193	191	183/189	183/187
D12S1048	214	214	214	214	214	211/214	214	214/223	214	214	223	211/214	211/226
D12S1301	112	116	120	120	116	116	116	108/116	100	120	116	100/116	100/100
D12S1701	95	97	91	91	95	95/97	97	95/101	92	91/95	95	97/101	91/97
Country of origin	**Norway**							**United States**			**Ireland**		**Poland**

Genotypes for probands from13 families with *LRRK2* G2019S are shown, those shared are highlighted in grey.

Figure 4. Probability of becoming affected by parkinsonism, in *LRRK2*G2019S carriers, as a function of age.



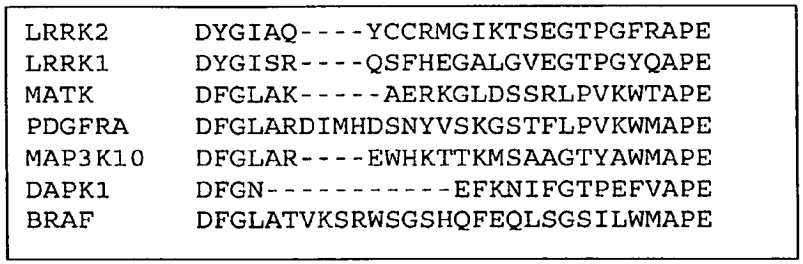


Figure 5. Aligned amino acid sequences of the activation loop of different human kinases.

In most kinases, the activation loop starts and ends with the conserved residues DFG and APE, respectively . In *LRRK2* and *LRRK1* phenylalanine is changed to tyrosine, an amino acid with a similar structure. (LRRK2 – leucine-rich repeat kinase 2, LRRK1 – leucine-rich repeat kinase 1, MATK – megakaryocyte-associated tyrosine kinase, PDGFRA – platelet-derived growth factor receptor alpha, MAP3K10 – mitogen-activated protein kinase kinase kinase 10, DAPK1 – death-associated protein kinase 1, BRAF – v-raf murine sarcoma viral oncogene homolog B1)